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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	23

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/623,035	Applicant(s) DURRANT ET AL.	
	Examiner MISOOK YU, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08-18-2003 and 11-20-2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,11,12 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,11,12 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence alginments*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08-18-2003 and 11/20/2003 have been entered.

Claims 1, 5-7, 11, 12, and 34 are amended, pending, and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejections.

Specification

The disclosure is newly objected to because of the following informalities: the specification at Fig. 9-11 and pages 31, line 17, middle of page 39 contain DNA and/or protein sequences that require SEQ ID NOs according to sequence rule. Applicant is kindly requested to look over the entire specification very carefully to see any other places might have sequences requiring SEQ ID NO. Sequence rule defined in 37 CFR 1.821 through 1.825 states each of unbranched specifically defined sequence of more than ten nucleotides or unbranched specifically defined sequence of four or more amino acids require a separate SEQ ID NOs (see MPEP § 2422). It appears that the paper copy and computer readable form copy applicant provided to the Office on 06-08-2001

contains SEQ ID NOs. Adding the corresponding SEQ ID NOs, for example, adding at the end of line 11 at page 39 of the specification "SEQ NO: 13" would obviate this objection.

Appropriate correction is required.

Claim Rejections - 35 USC § 102, Withdrawn

The rejection of the claim under 35 U.S.C. 102(b) as being anticipated by WO 89/01041 (02-09-1989) is withdrawn because the claims are no longer drawn to the full-length protein.

The Following Are New Grounds of Rejections and Objections

Claim Objections

Claim 34 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 34 is drawn to T cell epitope of the base claim and the base claim is already drawn to T cell epitope of the polypeptide of the CD55 family.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 5-7, 11, 12, and 34 are newly rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 5-7, 11, 12, and 34 as written, do not sufficiently distinguish over peptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by the specification at page 29. See MPEP 2105.

Claim Rejections - 35 USC § 112

Claims 1, 5-7, 11, 12, and 34 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is **new matter** rejection. The limitation of at least 7 to less than 30 is not supported by the specification at page 13, lines 20-27 because the specification states that the preferred fragments are 5-7, 7-9, 9-13, 20-30 and 30-40 and do not contemplate fragments of at least 7 to less than 30. Applicant are requested to provide specific support for the limitation in the specification as originally filed or remove it from the claims.

Claims 1, 5-7, 11, 12, and 34 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement requirement**. The claim(s)

contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is made because the specification fails to teach how to use the claimed 7-29-mer peptides for **inducing an anti-tumor T-cell immune response** without undue experimentation.

The specification teaches at pages 3-5, and 26-31 that CD55 (instant SEQ ID NO:2) is the antigen that the monoclonal antibody 791T/36 binds to. Based on this discovery along with the fact that the CDR regions of anti-idiotypic antibodies 105AD7 and have sequence homology to CD55, especially amino acid #83-93, 151-158, and 121-128 (note page 37 lines 16-28 of the specification), the specification asserts that 7-29-mer CD55 peptide sequence could be used as T-cell epitopes (see the paragraph bridging pages 5 and 6) for generating anti- tumor immunity. However, the specification fails to demonstrate the efficacy of the administered peptides or cells expressing said peptides on the induction of ant-tumor response, which reduces tumor burden or prevent the formation of a tumor in a patient. Searching potential T-cell epitopes in CD55 using existing software (this use is considered as research, not patentable use) does not require undue experimentation; the asserted actual patentable use is to use the claimed T-cell epitopes as immunogen for treating cancer. Undue experimentation is required to use the potential T-cell epitopes as immunogen to illicit anti-tumor response in a subject because the current state of art teaches that cancer therapy using CD55 derived T-cell epitopes. Durrant et al (1999, Cancer Research, vol. 59, pages 2282-6) at the last paragraph teaches the current status of CD55 for immunogen for

treating cancer i.e. CD55 **might be a possible target** for a "cancer vaccine" but its effectiveness as vaccine has not been proven and requires further study i.e."tumor cells overexpress CD55 to protect them from complement-mediated lysis or whether the enhanced level is related to an unknown function of this molecule is yet to be elucidated." Thus, Durrant et al teach that further research is necessary to see whether CD55 could be used as immunogen for cancer therapy. Further, Durrant et al (Curr Opin Investig Drugs. 2001 Jul; 2(7): 959-66, abstract only) teach CD-55 derived T-cell epitope effective to recognize CD55 overexpressing cancer cells have not been designed yet and requires careful consideration.

The specification fails to teach how administration of the claimed peptide would produce a sufficient amount of CTLs, NK cells and/or any other T cells to kill tumors in an animal or human that has malignant cells expressing CD55. Cancer therapy using immunogen is still unpredictable in the art. The specification teaches that SEQ ID NO:2 is a self antigen, rather than a mutated antigen, as it is expressed on normal tissues as well as cancerous tissues (see also Durrant et al, 1999, cited above), and that self-tolerance may eliminate T cells that are capable of recognizing these epitopes with high avidity (Sherman, LA et al, 1998, Critical reviews in Immunol, 18(1-2): 47-54, see especially at the abstract and Table 2). In other words, only CTLs with low affinity are left, which may not be optimal for tumor elimination *in vivo*. One of the problem is that after some period of time in the presence of tumor cells, T cells may lose their functional activity. Lauritzsen et al (International Journal of Cancer, 1998, Vol. 78, pp. 216-222) teach that clonal deletions of thymocytes is a major event in T-cell

tolerance which could lead to a tumor escape mechanism. In transgenic mice homozygous for HLA-specific CD+4 T-cells which are specific for a MOPC315 plasmacytoma, injection of a large number of tumor cells results in apoptosis of immature and mature transgenic CD+4+8 and CD+4 thymocytes. This negative selection was specific for the transgenic thymocytes that would complement the idiotype of the immunoglobulins of the MOPC315 plasmacytoma, because injection of tumor cells from a plasmacytoma which had a different idiotype of immunoglobulins failed to elicit the clonal deletion. Lauritzsen et al teach that injection of purified MOPC315 protein, versus the tumor cells, caused a profound reduction of the specific thymocytes specific to the idiotype of the plasmacytoma. Lauritzsen et al conclude that deletion of tumor specific thymocytes may represent a major escape mechanism in patients with cancers that secrete of shed antigens. In the instant case, the antigens are known self antigens. It would be reasonable to conclude that said normal antigens are presented within the thymus to developing thymocytes and T-cells with high affinity for said antigens are deleted as "self". It would be also reasonable to conclude that administration of the claimed polypeptides or cells expressing said polypeptides would not result in an efficacious vaccine as a T-cell response would not be evoked due to the process of clonal deletion in the thymus, rendering the host devoid of T-cells which are specific to the self-protein. Sarma et al (Journal of Experimental Medicine, 1999, Vol. 189, pp. 811-820) states that a critical issue in therapeutic regiments comprising the administration of tumor antigens for immunotherapy is whether unmutated tumor antigens which are expressed in normal cells impose special restrictions on the CTL

response in vivo. Using transgenic mice wherein the antigen specific T cells specific for the P1A non-mutated tumor antigen are expressed at high levels and remain responsive to the P1A antigen when assayed in vitro, it was found that P1A antigen expressed in the thymus resulted in clonal deletion of said specific T-cells Sarma et al note that although said transgenic mice produce an overwhelming majority of T cells that are specific for P1A, said mice are no more resistant to cells expressing P1A than non-transgenic litter mates. Sarma et al concludes that even thought P1A can be a tumor rejection antigen, the effector function of P1A specific CTL is restrained in vivo and that these results have important implications for the strategy of tumor immunotherapy. With regard to the isolation of two T-cells which are specific for the instant antigen presented in the context of HLA-A24, it cannot be determined if this is a reliable indicator that in all patients, with any of the types of cancers listed on page 20, would have a T-cell available after thymic selection which would react with said antigen in the context of HLA-A24 or any other MHC molecule.

The specification does not provided any evidence that any of the vast number of possible potential CD55 derived T-cell epitopes might be able to be used for cancer therapy. The specification does not disclose or suggest any other use of the claimed peptides other than cancers.

It is concluded based on the references discussed above, that the state of the art with respect to treating cancer patients of administering tumor antigens is unpredictable. The specification does not provide any disclosure that the administration of the claimed polypeptides would generate CTLs which lyse the cells of a tumor and it cannot be

predicted based on sequence homology to anti-idiotypic antibody to 791T/36. Considering the limited guidance, no working examples in the specification, and the unpredictability in the art, it is concluded that undue experimentation is required to use the claimed peptide an immunogen for anti-cancer therapy.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11, 12, and 34 are newly rejected under 35 U.S.C. **102(b)** as being anticipated by either US 5,264,357 (11-1993) or WO9406903-A1 (Mar. 31, 1994). .

The claims are interpreted as drawn to isolated peptides of 7 to 29 (claim 1), at least 9 (claim 11), at least 13 (claim 12) contiguous amino acids from SEQ ID NO:2, wherein said peptides contain a T cell epitope of the base claim (claim 34).

US 5,264,357 teaches an isolated peptide consisting of 22 amino acids that match amino acids 35 to 56 of instant SEQ ID NO:2, thus anticipating the structural element of instant claims 1, 11, 12, and 34. Note the attached sequence alignment.

WO9406903-A1 teaches an isolated peptide consisting of 29 amino acids that match amino acids 353 to 381 of instant SEQ ID NO:2, thus anticipating the structural element of instant claims 1, 11, 12, and 34. Note the attached sequence alignment.

Claims 1, and 34 are also newly rejected under 35 U.S.C. **102(b)** as being anticipated by US 5,545,619 (08-1996).

The claims are interpreted as drawn to isolated peptides of 7 to 29 of instant SEQ ID NO:2, which is a T cell epitope.

US 5,545,619 teaches an isolated peptide consisting of 8 amino acids that match amino acids 214 to 221 of instant SEQ ID NO:2, thus anticipating the structural element of instant claims 1, and 34. Note the attached sequence alignment, thus anticipating the structural element of instant claims 1 and 34. Note the attached sequence alignment.

Determining whether the sequences of the prior art possess the function i.e., capable of being used as a T-cell epitope requires experiments. However, the Office does not have facilities to perform such experiments, therefore cannot provide the factual evidence needed in order to establish that the sequences of the prior art are not T-cell epitopes. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed protein sequences are different from those taught by the prior art and to establish patentable differences. Note See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-

308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
January 21, 2004

LARRY R. HELMS, PH.D
PRIMARY EXAMINER